Claims

1. A method of making a silicone rubber having a structure adapted for growth of cells or living tissue, which comprises contacting a silicone rubber precursor with a biologically-acceptable sacrificial filler, curing the resultant mixture and removing the sacrificial filler to form a structured silicone rubber.

2. A method as claimed in claim 1, wherein the silicone rubber precursor can be cured or vulcanized at room temperature.

3. A method as claimed in claims 1 or 2, wherein the biologically-acceptable sacrificial filler is bio-compatible, such that it is innately non-toxic and does not leave a toxic residue.

4. A method as claimed in claims 1, 2 or 3, wherein the sacrificial filler does not interact chemically with the silicone rubber precursor or with the resultant silicone rubber and is stable at temperatures used to cure the resultant mixture.

5. A method as claimed in any one of the preceding claims, wherein the sacrificial filler is granular and, preferably, crystalline.

6. A method as claimed in any one of claims 1-4, wherein the sacrificial filler is amorphous.

7. A method as claimed in any one of the preceding claims, wherein the sacrificial filler is ground and, preferably, classified, prior to contacting the silicone rubber precursor.

8. A method as claimed in claim 7, wherein the sacrificial filler is wet-milled, prior to mixing with the silicone rubber precursor.

9. A method as claimed in claims 7 or 8, wherein the sacrificial filler is milled to a particle size of 0.01-10 μm, preferably 0.05-1 μm, and most preferably 0.1-0.4 μm.

10. A method as claimed in claims 8 or 9, wherein the sacrificial filler is an inorganic salt and is milled in an organic solvent.

11. A method as claimed in any one of the preceding claims, wherein the sacrificial filler is an inorganic salt selected from the group consisting of metal halides, metal carbonates and metal bicarbonates.

12. A method as claimed in claim 11, wherein the inorganic salt is selected from the group consisting of lithium bicarbonate, sodium bicarbonate, potassium bicarbonate, lithium chloride, sodium chloride and potassium chloride.

13. A method as claimed in claim 12, wherein the sacrificial filler is sodium bicarbonate or sodium chloride, preferably food grade sodium bicarbonate or sodium chloride.

14. A method as claimed in claim 13, wherein the sodium bicarbonate or sodium chloride is wet-milled under xylene.

15. A method as claimed in any one of the preceding claims, wherein the sacrificial filler is removed by dissolution, preferably in an aqueous solvent.

16. A method as claimed in claim 15, wherein the sacrificial filler does not cause swelling of the silicone rubber when removed using an aqueous solvent.

17. A method as claimed in claim 16, wherein the sacrificial filler is sodium bicarbonate.

18. A method as claimed in any one of the preceding claims, wherein free –OH groups of the silicone rubber are chemically modified, so as to enhance cell adherence.

19. A method as claimed in any one of the preceding claims, wherein the surface of the silicone rubber is charged by bombardment with electrons.

20. A method as claimed in any one of the preceding claims, wherein the silicone rubber precursor comprises at least one additive that is not removed with the sacrificial filler and serves to impart desired physical properties on the rubber.

21. A method as claimed in claim 20, wherein the additive is a metal powder or carbon black and serves to render the silicone rubber electrically conductive.

22. A method as claimed in claim 21, wherein the additive is stainless steel powder.

23. A method as claimed in claim 21, wherein the additive is iron oxide.

24. A method as claimed in claim 20, wherein the additive is an inert substance, such as glass, and serves to render the silicone rubber mechanically rigid.

25. A method as claimed in any one of the preceding claims, wherein a surface of the silicone rubber precursor is contacted with the sacrificial filler, so as to form a structured silicone rubber having a textured surface.

26. A method as claimed in claim 25, wherein the textured surface of the silicone rubber facilitates attachment of adherent cells.

27. A method as claimed in claims 25 or 26, wherein the textured surface of the silicone rubber provides an increased number of sites for attachment of cells relative to an untextured surface.

28. A method of making a textured silicone rubber as claimed in claims 25, 26 or 27, which comprises forming a coating of a silicone rubber precursor on a substrate, contacting a surface of the coating with a biologically-acceptable sacrificial filler, curing the resultant mixture and removing the sacrificial filler to form a textured silicone rubber.

29. A method as claimed in claim 28, wherein the surface of the coating is contacted with the sacrificial filler under pressure, such that the sacrificial filler is substantially completely embedded in the coating.

30. A method as claimed in claim 29, wherein the sacrificial filler is embedded to a depth of 0.1-1.0 mm, preferably 0.1-0.5 mm, and most preferably 0.1-0.25 mm.

31. A method as claimed in claim 30, wherein the sacrificial filler is scattered or sprinkled over the surface of the coating, such that the sacrificial filler is only partially embedded in the surface.

32. A method as claimed in any one of claims 25-31, wherein the textured surface is micro-cupulated, the micro-cupules having a depth of less than 1 mm, preferably a depth of 0.5-0.1 mm.

33. A method as claimed in claim 32, wherein the micro-cupules measure less than 2 mm across, preferably less than 1 mm across, and, most preferably, less than 0.5 mm across.

34. A method as claimed in any one of claims 1-24, wherein the sacrificial filler is dispersed throughout the silicone rubber precursor, and the structured silicone rubber is substantially porous.

35. A method as claimed in claim 34, wherein the pores of the silicone rubber provide sites of attachment for cells or tissues, so that the cells or tissues may be substantially trapped within the resultant structure.

36. A method of making a porous silicone rubber as claimed in claims 34 or 35, which comprises mixing the biologically-acceptable sacrificial filler with the silicone rubber precursor, curing the resultant mixture at a temperature below 180°C, and removing the sacrificial filler, to form a porous silicone rubber.

37. A method as claimed in claims 34, 35 or 36, wherein the resultant mixture is shaped prior to curing, preferably by moulding or extrusion.

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38. A method as claimed in any one of claims 34-37, wherein the pores are 1 μm-0.5 mm, preferably 10 μm to 0.2 mm, and most preferably 50 to 150 μm in diameter.

39. A method as claimed in any one of claims 34-38, wherein the porous silicone rubber is cut to a desired size or shape.

40. A method of making a textured or porous silicone rubber substantially as hereinbefore described with reference to the accompanying drawings.

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41. A textured or porous silicone rubber obtained or obtainable by a method according to any one of the preceding claims.

42. A textured or porous silicone rubber substantially as hereinbefore described with reference to the accompanying drawings.

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43. A biomedical device or apparatus comprising a textured or porous silicone rubber as claimed in claims 41 or 42.

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44. A culture chamber for use in a method of culturing microbiological material, which comprises at least one gas-permeable wall or portion of a wall, and a textured interior growth surface arranged for contact with the microbiological material being cultured.

45. A culture chamber as claimed in claim 44, wherein the gas-permeable wall and the textured interior growth surface are each formed from an organic polymer.

46. A culture chamber as claimed in claim 45, wherein the gas-permeable wall and the textured interior growth surface are formed of the same organic polymer.

47. A culture chamber as claimed in claims 44, 45 or 46, wherein the at least one gas-permeable wall or portion of a wall also provides the textured interior growth surface.

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48. A culture chamber as claimed in any one of claims 44-47, wherein the textured interior growth surface is a textured silicone rubber obtained or obtainable by a method according to any one of claims 25-33.

49. A culture chamber as claimed in any one of claims 44-48, wherein the at least one gas-permeable wall or portion of a wall is a silicone rubber membrane.

50. A culture chamber as claimed in any one of claims 44-49, including at least one port extending between the interior and the exterior of the chamber.

51. A culture chamber as claimed in claim 50, including an inlet port and an outlet port.

52. A culture chamber as claimed in claims 50 or 51, including at least one septum port.

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53. A culture chamber as claimed in any one of claims 44-52, in the form of a flexible bag or envelope, preferably made of silicone rubber.

54. A culture chamber as claimed in any one of claims 44-53, including a valve means for release of gasses that build up within the chamber during use.

55. A culture chamber as claimed in claim 54, wherein the valve means comprises at least one filter means, the filter means allowing gasses to diffuse out of the chamber, but preventing microbial contamination thereof.

56. A culture chamber as claimed in claims 54 or 55, wherein the valve means comprises one or more layers of a hydrophobic porous material.

57. A culture chamber as claimed in claim 56, wherein the hydrophobic membrane is a PTFE membrane having a thickness of 0.25 mm and a porosity of 0.2 μm.

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58. A culture chamber as claimed in any one of claims 44-57, further comprising a second chamber separated from the first chamber by means of a semi-permeable membrane.

59. A culture chamber as claimed in claim 58, wherein the second chamber has an access means separate from that of the first chamber.

60. An apparatus comprising a plurality of culture chambers as claimed in any of claims 44-59, for use in a method of culturing microbiological material.

61. An apparatus as claimed in claim 60, wherein the inlets of the culture chambers are interconnected and the outlets of the culture chambers are interconnected.

62. An apparatus as claimed in claims 60 or 61, wherein a further chamber having a semi-permeable wall is positioned within each culture chamber, each semi-permeable chamber having an inlet that is interconnected with the inlet of the other semi-permeable chambers and having an outlet that is interconnected with the outlet of the other semi-permeable chambers.

63. An apparatus as claimed in claim 62, wherein said apparatus is a bio-reactor.

64. A method of culturing microbiological material in a culture chamber as claimed in any one of claims 44-59, or an apparatus as claimed in any one of claims 60-63.

65. A method as claimed in claim 64, comprising growing anchorage-dependent stromal cells on the textured surface of the culture chamber(s), and then innoculating anchorage-independent stem cells into the culture chamber(s), to allow proliferation of the stem cells.

66. A method of carrying out a bio-processing operation in a culture chamber or an apparatus as claimed in any one of claims 44-63, which comprises attaching cells for performing the bio-processing function to the textured surface of the culture chamber(s), introducing liquor to be processed into the culture chamber(s) *via* an inlet and collecting the processed liquor at an outlet from the culture chamber(s).

67. A method as claimed in claim 66, which comprises culturing cells on the textured surface in a culture medium, removing spent medium including cellular by-products from the culture chamber(s), and passing fresh nutrient medium through a semi-permeable chamber(s) located within the culture chamber(s), so to allow fresh medium to diffuse through the semi-permeable membrane into the culture chamber(s).

68. A method as claimed in claim 67, wherein the nutrient medium is passed through the semi-permeable chamber in the opposite direction to that in which the liquor or spent medium is passed through the culture chamber.

69. A method as claimed in claims 67 or 68, wherein the nutrient medium is recycled.

70. A well for use in a method of culturing microbiological material and having at least one wall defining the well, at least a portion of the wall being gas-permeable to enhance oxygen supply to the well, and at least a portion of the interior surface of the wall being textured to increase surface area and to enhance cell adherence.

71. A well as claimed in claim 70, wherein the gas-permeable portion of the wall and the textured portion of the wall are positioned at the base of the well.

72. A well as claimed in claims 70 or 71, wherein the gas-permeable portion of the wall comprises a gas-permeable membrane, preferably formed of silicone rubber.

73. A well as claimed in claims 71 and 72, wherein the membrane has a textured surface facing the interior of the well.

74. A well as claimed in any one of claims 70-73, wherein the textured surface has crater-like depressions or micro-cupules.

75. A well as claimed in any one of claims 70-74, wherein the textured surface is made by a method as claimed in any one of claims 25-33.

76. A microtitre plate having at least one well as claimed in any one of claims 70-75.

77. A method of culturing microbiological material on a well as claimed in any one of claims 70-75, or into a microtitre plate as claimed in claim 76.

78. An implant device comprising a cell support structure having a coating with a textured surface, to promote anchorage of the implant by cell attachment and ingrowth by surrounding tissue upon implant.

79. An implant device as claimed in claim 78, wherein the textured surface has crater-like depressions or micro-cupules.

80. An implant device as claimed in claims 78 or 79, wherein the coating comprises textured silicone rubber.

81. An implant device as claimed in claim 80, wherein the textured silicone rubber coating is made by a method as claimed in any one of claims 25-33.

82. An implant device as claimed in any one of claims 78-81, wherein the device is a heart valve, a sternum implant, or a reconstructed calf ligament.

83. A substrate for growth of skin grafts *in vitro*, comprising a flexible membrane having a textured surface.

84. A substrate as claimed in claim 83, wherein the flexible membrane prevents the skin graft from becoming brittle, whilst the textured surface increases the surface area for cell adhesion, promotes cell adhesion and gives the skin a rough surface to enhance "taking" of the graft on transplant.

85. A substrate as claimed in claims 83 or 84, wherein the flexible membrane is gas-permeable.

86. A substrate as claimed in claim 85, wherein the membrane comprises silicone rubber.

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87. A substrate as claimed in any one of claims 84-86, wherein the textured surface has crater-like depressions or micro-cupules.

88. A substrate as claimed in any one of claims 84-87, wherein the textured surface is a textured silicone rubber made by a method as claimed in any one of claims 25-33.

89. A skin graft grown on a substrate as claimed in any one of claims 84-88.

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90. A tissue support structure for use in a method of culturing tissue or cellular agglomerates, which comprises a biocompatible material having an internal system of pores, the pores promoting cell attachment and anchorage and oxygen supply to the tissue.

91. A tissue support structure as claimed in claim 90, wherein the porous material is provided with small, fine bore tubes.

92. A tissue support structure as claimed in claims 90 or 91, wherein the shape of the porous material is adapted so as to engineer the shape of the resultant tissue.

93. A tissue support structure as claimed in claim 90, wherein the porous material comprises porous silicone rubber.

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94. A tissue support structure as claimed in claim 93, wherein the porous silicone rubber is made by a method as claimed in any one of claims 34-39.

95. An apparatus for culturing tissue or cellular agglomerates, comprising a tissue support structure as claimed in any one of claims 90-94, wherein the apparatus further comprises a gas-permeable membrane, to enhance oxygen supply to the system of pores and channels within the porous material, and therefore to the tissue.

96. An apparatus as claimed in claim 95, wherein the gas-permeable membrane is attached to the porous material.

97. An apparatus as claimed in claim 96, wherein the gas-permeable membrane comprises silicone rubber.

98. An apparatus as claimed in claims 96 or 97, wherein the porous material is attached to the gas-permeable membrane using a gas-permeable adhesive.

99. An apparatus as claimed in claim 98, wherein the gas-permeable adhesive is a silicone rubber adhesive.

100. An apparatus as claimed in any one of claims 94-99, wherein a plurality of tissue support structures are arranged in close proximity to one another, so as to allow fusion between tissue or cell masses growing on each structure, to create larger tissue or cellular agglomerates.

101. An artificial implant formed from a material having an internal system of pores, the pores promoting cell attachment and anchorage and oxygen supply to the cells on the implant surface.

102. An artificial implant as claimed in claim 101, wherein the porous material comprises porous silicone rubber.

103. An artificial implant as claimed in claim 101, wherein the porous material is made by a method as claimed in any one of claims 34-39.

104. An artificial implant as claimed in claims 101, 102, or 103, for use as a cartilage implant.

105. A cartilage implant as claimed in 104, wherein the porous material has been seeded *in vitro* with chondrocites, to form a layer of cartilage over the implant.

106. A cartilage implant as claimed in claims 104 or 105, for replacing eroded joints, wherein the porous silicone structure has been moulded to conform to the shape of the bone, which it is to protect.

107. A cartilage implant as claimed in claims 104, 105 or 106, wherein the porous material has been moulded into the shape of a nasal bridge.

108. A cartilage implant as claimed in claims 104, 105 or 106, wherein the porous material has been moulded into the shape of an ear.

109. An artificial implant as claimed in any one of claims 101, 102, or 103, for use as a vascular graft.

110. A vascular graft as claimed in claim 109, comprising a hollow tube made from porous material, preferably porous silicone rubber.

111. A vascular graft as claimed in claims 109 or 110, further providing an interior surface for cell adhesion.

112. A vascular graft as claimed in claim 111, wherein endothelial cells are grown on the interior surface of the graft.

113. A vascular graft as claimed in claims 111 or 112, providing an exterior surface for cell adhesion.

114. A vascular graft as claimed in claim 113, wherein smooth muscle cells are grown on the exterior surface of the graft.

115. A vascular graft as claimed in any one of claims 109-114, wherein one or both surfaces of the graft are additionally roughened to enhance cell attachment, preferably by providing the graft with textured silicone rubber surface.

116. A cell implant means comprising a porous material for retention of cells to be implanted, the pores promoting cell attachment and anchorage and oxygen supply to the cells, and a protective means to shield the cells from immune attack after implant.

117. A cell implant means as claimed in claim 116, wherein the porous material comprises silicone rubber.

118. A cell implant means as claimed in claim 117, wherein the porous silicone rubber is made by a method as claimed in any one of claims 34-39.

119. A cell implant means as claimed in claims 116, 117 or 118, wherein the protective means comprises a semi-permeable membrane forming an envelope around the porous material.

120. A cell implant means as claimed in any one of claims 116-119, for use as an endocrine implant.

121. An endocrine implant as claimed in claim 120, wherein the porous material is seeded *in vitro* with endocrine cells.

122. An endocrine implant as claimed in claim 121, wherein the endocrine cells are islets of Langerhans cells.

123. A drug delivery system comprising a porous material whose pores have been impregnated or saturated with a drug for delivery.

124. A drug delivery system as claimed in claims 123, suitable for implantation into a human or animal body.

125. A drug delivery system as claimed in claims 123 or 124, wherein the drug is present in admixture with at least one sustained release ingredient.

126. A drug delivery system as claimed in claims 123, 124 or 125, wherein the porous material comprises a porous silicone rubber.

127. A drug delivery system as claimed in claim 126, wherein porous silicone rubber is made by a method as claimed in any one of claims 34-39.

128. A filtration media comprising porous silicone rubber, for use in separations.

129. A filtration media as claimed in claim 128, wherein the porous silicone rubber is made by a method as claimed in any one of claims 34-39.

130. A filtration media as claimed in claims 128 or 129, wherein the pores in the silicone rubber are of sub-micron size, preferably in the order of 0.1 – 0.5 μm.

131. A filtration media as claimed in claims 128, 129 or 130, for use in magnetic separation.

132. A filtration media as claimed in claim 131, wherein the porous silicone rubber includes magnetic additives.

133. A filtration media as claimed in any one of claims 128-132, for use in expanded bed absorption.

134. A filtration media as claimed in claim 133, wherein the porous silicone rubber is in particulate form.

135. A filtration media as claimed in any one of claims 128-134, for use in static inline filtration.

136. A filtration media as claimed in claim 135, wherein the porous silicone rubber is in the form of sheets or tubes.

137. A filtration media as claimed in any one of claims 128- 136, wherein the porous silicone rubber is in the form or annular discs.

138. A cell cryopreservation system, comprising a porous material for absorbing cell culture into the internal system of pores and a container suitable for storage in liquid nitrogen.

139. A cell cryopreservation system as claimed in claim 143, wherein the porous material comprises porous silicone rubber.

140. A cell cryopreservation system as claimed in claim 139, wherein the porous silicone rubber is made by a method as claimed in any one of claims 34-39.

141. A cell cryopreservation system as claimed in claims 138, 139 or 140, wherein the container comprises releasable sealing means.

142. A cell cryopreservation system as claimed in claim 141, wherein the container is a syringe-type plunger.

143. An electrode comprising a porous material having electrically conductive particles dispersed therein.

144. An electrode as claimed in claim 143, wherein the porous material comprises porous silicone rubber.

145. An electrode as claimed in claim 144, wherein the porous silicone rubber is made by a method as claimed in any one of claims 34-39.

146. An electrode as claimed in claims 148, 149 or 150, wherein the conductive particles are metal or carbon powders.

147. An electrode as claimed in any one of claims 143-146, wherein the porosity of the material promotes adherence of microorganisms to the electrode surface, preferably microorganisms that are capable of digesting waste.

148. An electrode system comprising a plurality of electrodes as claimed in any one of claims 143-147 immersed in a liquid electrolyte and connected to an electric circuit.

149. A method of treating sewage using an electrode system as claimed in claim 148.

150. A wound dressing comprising a first layer of a porous gel and a second layer of a carrier gel.

151. A wound dressing as claimed in claim 150, wherein the porous gel layer comprises porous silicone rubber gel, preferably made by a method as claimed in any one of claims 34-39.

152. A wound dressing as claimed in claims 150 or 151, wherein the carrier gel layer comprises a silicone gel.

153. A wound dressing as claimed in claims 150, 151 or 152, wherein the carrier gel is applied to a supportive structure, preferably a Dacron® mesh.

154. A wound dressing as claimed in any one of claims 150-153, wherein the porous gel layer is infused with a drug for delivery to the wound.

155. A wound dressing as claimed in claim 154, wherein the drug is a growth-promoting drug.

156. A wound dressing as claimed in claim 155, wherein the drug is an antibiotic.

157. A clinical swab, comprising a porous material, the pores increasing the surface area of the swab and promoting oxygen transport to the swab surface.

158. A clinical swab as claimed in claim 157, wherein the porous material comprises porous silicone rubber.

159. A clinical swab as claimed in claim 158, wherein the porous silicone rubber is made by a method as claimed in any one of claims 34-39.

160 A clinical swab as claimed in claims 157, 158 or 159, wherein the porous material contains a radio-opaque additive, preferably barium sulphate.

161. A clinical swab as claimed in any one of claims 157-160, wherein the porous material is infused with a drug.